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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,410	07/10/2001	Dan E. Robertson	DIVER1180-2	8980

28213 7590 02/11/2004

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,410	ROBERTSON ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23,40-55,61-63,65,67,68,73-85 and 88-109* is/are pending in the application.

4a) Of the above claim(s) *42-55,61-63,65 and 88-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23,40,41,67,68,73-85 and 93-109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 24-39, 56-60, 64, 66, 69-72, 86 and 87 have been canceled. Claims 1-23, 40-55, 61-63, 65, 67, 68, 73-85, 88-102 and newly presented claims 103-109 are still at issue and are present for examination.

Applicants' arguments filed on 11/21/03, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 42-55, 61-63, 65 and 88-92 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed 6/2/03. Applicants are advised to use the claim identifier (withdrawn) for all non-elected claims in all future responses even if the claims are being amended therein.

Applicant is advised that should claim 79 be found allowable, claim 104 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the

other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The claims are identical.

Claims 2-5, 19-21, 67, 68, 73-81, 83, 84, 97, 99, 104, 105, and 109 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is confusing in the recitation of "comprising a sequence comprising SEQ ID NO:26 and sequences complementary thereto" as applicants deleted the phrase "selected from the group consisting of". As such it is unclear if the claim is intended to be limited to only nucleic acids having both a sequence comprising SEQ ID NO:26 and its complement present (i.e., a double stranded DNA) or if applicants intended meaning was "comprising a sequence of SEQ ID NO:26 or sequences complementary thereto". It is presumed that "or" was intended. Claims 3-5 are similarly confusing in the recitation of "hybridizing to a nucleic acid comprising (a) a sequence having at least 70% sequence identity to SEQ ID NO:26 and encoding a polypeptide having an esterase activity and (b) sequences complementary to (a)". It is assumed that "or" was intended.

Claims 19-21 are confusing in the recitation "wherein the sequence identity is at least about X%" as it fails to identify

what the reference sequence is. For purposes of examination it is assumed that "wherein the sequence identity is at least about X% to SEQ ID NO:26" was intended.

Claims 67 (upon which claims 68, 73-81, 104 and 105 depend), 83, 84 and 97 are indefinite in the recitation of "at least about 30, 35, 40, 45, 50, 75, 100, 150, or 200 nucleotides in length" as it makes the length of the recited oligonucleotides encompassed vague and confusing". For purposes of examination this entire recitation is interpreted as "at least 30 nucleotides". Furthermore Claims 79, 104, and 105 are further confusing in reciting lengths of less than 10-50 bases while the claims from which they depend recite minimum lengths of 30 bases.

Claims 73-78 are indefinite in the recitation of "% sequence identity to the nucleic acid" as it is unclear what nucleic acid is being referenced. For purposes of examination it is presumed that "% sequence identity to SEQ ID NO:26" was intended.

Claim 99 is confusing in the inclusion of "a fosmid" in the recited Markush group is not understood as these are not known types of vectors. Applicants submit that fosmid vectors were well known in the art at the time of the invention and submitted the abstract of Kim (1995) in support of this. However, while the Kim abstract uses the term it does not explain what it means and it is not clear from the abstract that this is an art

accepted term with a known meaning. It should be noted that the examiner cannot find the term in the Oxford Dictionary of Biochemistry and Molecular Biology, 2002 edition (A.D. Smith, Oxford University Press).

The term "thermostable" in claim 109 is a relative term which renders the claim indefinite. The term "thermostable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what temperature the esterase must be stable to and still retain activity to be within the scope of this term.

Claims 107-109 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as filed does not appear to provide support for the limitations of new claims 107-109. Specifically the specification does not appear to provide support for the esterase activity being limited to "catalysis of a

transesterification reaction" or "catalysis of a acidolysis reaction" nor for the encoded esterase being thermostable.

Claims 1, 3-23, 40, 41, 67, 68, 73-85, and 93-109 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is explained in the previous Office Action.

Applicants submit that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that applicants were in possession of the claimed invention. In support of applicants position applicants refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. 112 first paragraph, specifically example 14, in which a claim reciting variants is claimed by sequence identity and function (i.e. catalyze the reaction of A to B). Based on this example, applicants suggest that these guidelines recognize that the written description requirement is met for a genus of polynucleotides described by a physico-chemical property and a defined function, and thus applicants conclude that the genus of

claimed polynucleotides also meet the written description requirements of 112. Applicants argument is not found persuasive for the following reasons. First it should be pointed out that the vast majority of the claims have no functional limitations at all. None of Claims 3-21, 23, 41, 67-85, 93-102, 104, and 105 require the claimed nucleic acids to encode an esterase or have any other functional limitation present. As such applicants analogy to example 14 for these claims is totally inconsistent. The remaining rejected claims (i.e., 1, 22, 40, 103, and 106-109) do require the claimed nucleic acids to encode an esterase and thus do have a both a structural and functional limitation as found in Example 14 of the guidelines. However, "esterase activity" encompasses a highly diverse genus of activities as the term esterase is generic to a large number of distinct activities. Virtually all esterases are known have activity on only certain types of esters. As such the claimed genus is diverse in functional features and different from example 14 of the guidelines in which the claim is clearly limited to only variants which catalyze a specific chemical reaction. As the claimed genus is diverse in function, the single species within said genus disclosed in the specification (i.e., SEQ ID NO:26) is not representative of the entire genus. Finally it should be noted that many of the claims also lack sufficient structural

limitations as well. As stated by applicants the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997) may be achieved by a recitation of a representative number of DNAs defined by nucleotide sequence or a recitation of structural features common to members of the genus, which features **constitute a substantial potion of the genus**. Claims 5-9, 11-14, 16-21, 23, 41, 67-85, 93-102, 104, and 105 all recite nucleic acids which comprise only 30 nucleotides of SEQ ID NO:26, encoding only 30 amino acids of SEQ ID NO:36 or having less than 40% overall sequence identity to SEQ ID NO:26 as the only recited structural limitations of the claims. These recited structural features of the genus (even if a limitation to encoding esterase activity is present) do not constitute a substantial potion of the genus as the remainder of the structure of a nucleic acid encoding a polypeptide with esterase is completely undefined. Fragments consisting of only 30 nucleotides of SEQ ID NO:26, encoding 30 amino acids of SEQ ID NO:36 or having less that 40% identity to SEQ ID NO:26 are highly unlikely to have esterase activity, constitute only a very small portion of the structure of the only disclosed species (SEQ ID NO:26) and the specification does not define the remaining

structural features necessary for members of the genus to be selected.

Claims 1, 3-23, 40, 41, 67, 68, 73-85, and 93-109 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding SEQ ID NO:36, does not reasonably provide enablement for any polynucleotide having at least 50% (or 70%) sequence identity to SEQ ID NO:26 and encoding a polypeptide with an esterase activity or any polynucleotide comprising at least 30 bases of a sequence having 70% identity to SEQ ID NO:26 and encoding a polypeptide having esterase activity, or any polynucleotide comprising a fragment of SEQ ID NO:26 or encoding fragments of SEQ ID NO:36, or all fragments and variants thereof or vectors and host cells comprising said nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is explained in the previous Office Action.

Applicants argue that the specification enabled the skilled artisan at the time of the invention to identify, make and use the genus of esterases claimed. Applicants refer to a declaration by inventor Jay Short, who declares that the state of the art at the time of the invention and the level of skill of

the person of ordinary skill in the art was very high. Dr Short's declaration further states that one of skill in the art at the time of the invention could use the teachings of the specification and other protocols known in the art to screen for polypeptides having esterase activity and that while the number of samples needed to be screened may have been high, the screening procedures were routine and successful results predictable. According to Dr. Short's declaration, knowledge of the specific structural elements which correlate with esterase activity would not have been required to create variants and test them for activity. Applicants further argue that enablement is not precluded by the necessity to screen large number of compositions as long as that screening is routine. Applicants refer to *Hybritech, Inc. v. Monoclonal Antibodies, Inc.* as support for the argument that the claimed invention is enabled even if there is a need to screen large numbers of negatives to find a sample with the desired activity.

As indicated in the previous Office Action, the specification is completely silent in regard to which are the amino acid residues which can be substituted, deleted, or inserted in the nucleic acid of SEQ ID NO:26 to obtain structural homologs of the nucleic acid of SEQ ID NO:26 as recited in the

claims which encode proteins with esterase activity. In addition, the specification does not provide any clue as to which 30 consecutive base fragments of the nucleic acid of SEQ ID NO:26 are required to encode proteins with esterase activity nor does it provide any clue as to which fragments of a nucleic acid having at least 70% sequence identity to the SEQ ID NO:26 and encoding an esterase are essential for esterase activity. Moreover, no teaching or suggestion has been presented in regard to the critical structural elements required in a polypeptide to catalyze the enzymatic hydrolysis of any ester. The prior art clearly teaches the unpredictability of assigning function based on structural homology and how small structural changes can lead to major changes in function. For specific teachings of such unpredictability, see Bork, Broun et al., Van de Loo et al., Witkowski et al. and Seffernick et al. Each of these references which are presented merely as evidence of the state of the art as previously characterized by the examiner, shows that even small changes in the primary structure of an encoded protein can have substantial effects on function. Furthermore, it should be noted that applicants claims encompass not only nucleic acids having minor changes in structure from SEQ ID NO:26, but include nucleic acids with major changes as well. Therefore, in the absence of

any information as to how structure correlates with function, one of skill in the art would have to go through the burden of undue experimentation to isolate/make the nucleic acids as encompassed by the claims, to practice the full scope of the claimed invention.

The Examiner acknowledges the ruling in *Hybritech, Inc. v. Monoclonal Antibodies, Inc* as well as the declaration by inventor Jay Short, and agrees that enablement is not precluded by the need of screening a number of compositions as long as the screening is routine. Furthermore, the Examiner agrees that creation of nucleic acids having the structural limitations recited in the claims is routine in the art. However, the Examiner disagrees with Applicant's contention that testing the extremely large number of variants encompassed by the claims is not undue experimentation when there is no guidance or knowledge as to which are the structural elements in the polypeptide encoded by SEQ ID NO:26 that correlate with enzymatic hydrolysis of any ester. It is not routine in the art to randomly create an infinite number of variants and test them for activity. Instead, as indicated above, one of skill in the art would have some knowledge or guidance as to how structure correlates with function such that a reasonable number of variants with the

potentiality of having the desired function can be created and tested. Thus, in view of the information provided, the lack of relevant examples, the lack of knowledge about the critical structural elements required for enzymatic hydrolysis of any ester, and the unpredictability of the art in regard to accurate annotation of function based on structural homology, one of skill in the art cannot reasonably conclude that the specification is enabling for the full scope of the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 5-15, 67-84, 93-97, 103-105 and 107-109 rejected under 35 U.S.C. 102(b) as being anticipated by Robertson et al. (WO 97/30160). The rejection is explained in the previous Office Action.

Applicants argue that the priority document inherently supports claims directed to nucleic acids having 50%, 55%, 60%, 65% or more sequence identity to the exemplary SEQ ID NO:26, or the nucleic acid encoding SEQ ID NO:36. Applicants argue that the priority document states that "in accordance with one aspect of the present invention, there are provided novel enzymes, as

well as active fragments, analogs and derivatives thereof" and also states that "the present invention also relates to nucleotide changes which result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference polynucleotide. In a preferred aspect of the invention these polypeptides retain the same biological action as the polypeptide encoded by the reference polynucleotide" and further states that "numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, within the scope of the appended claims, the invention may be practiced otherwise than as particularly described". Applicants argue that it is well established that there does not have to be *ipsis verbis* support in the specification and that what is necessary is that one of skill in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented. This is acknowledged but is **exactly** the problem in the instant case. One of skill in the art reading the specification as filed would **not** have recognized that applicants considered the currently claimed genera and sub-genera to be their invention. While the claimed sub-genera are clearly within the scope of the extremely broad and vague recitation of the

parent application of "novel enzymes, as well as active fragments, analogs and derivatives thereof" and "nucleotide changes which result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference polynucleotide" quoted by applicants these passages in no way would have transmitted to an ordinary artisan that applicants considered the currently claimed sub-genera to be their invention. It is well established that a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads (see MPEP 2163). As such the parent application does not provide support for the limitations of the currently rejected claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened

statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Rebecca Prouty
Primary Examiner
Art Unit 1652